

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

BHASKARAN et al.

Appl. No.: 10/743,295

Filed: December 23, 2003

For: Polymer Conjugates of Cytokines,

Chemokines, Growth Factors, Polypeptide Hormones and

Antagonists Thereof with Preserved

Receptor-Binding Activity

Confirmation No.: 7998

Art Unit: 1641

Examiner: To Be Assigned

Atty. Docket: 2057.0060002/JAG/BJD

Information Disclosure Statement under 37 C.F.R. § 1.97(b)

Commissioner for Patents PO Box 1450 Alexandria, VA 22313-1450

Sir:

Listed on accompanying Form PTO-1449 are documents that may be considered material to the examination of this application, in compliance with the duty of disclosure requirements of 37 C.F.R. §§ 1.56, 1.97 and 1.98. Copies of the documents are submitted herewith.

No copies of U.S. patents and patent application publications cited on the attached Form PTO-1449 are submitted herewith in accordance with 1276 OG 55, because this application was filed after June 30, 2003.

In accordance with 37 C.F.R. § 1.98(a)(3)(i), Applicants' undersigned representative submits the following concise explanation of the non-English language document AP4 cited on Form PTO-1449:

Document AP4, PCT Patent Publication No. WO 04/046222 A1, is in the Japanese language. An English language abstract of document AP4 appears on its face page.

Applicants would like to bring to the Examiner's attention documents AR30, Schein, C.H., and AS35, Youngster, S., for which the month of publication could not be determined after diligent attempts. Applicants note that the first filing date in the present matter is December 26, 2002, which would imply that all documents published in 2001 and later should have the month of publication listed on the Form PTO-1449 as well. If the Examiner has information indicating the month of publication of either or both of documents AR30 and/or AS35, Applicants respectfully request that that information be made of record in the present matter.

Where the publication date of a listed document does not provide a month of publication, the year of publication of the listed document is sufficiently earlier than the effective U.S. filing date and any foreign priority date so that the month of publication is not in issue. Applicants have listed publication dates on the attached PTO-1449 based on information presently available to the undersigned. However, the listed publication dates should not be construed as an admission that the information was actually published on the date indicated.

Applicants reserve the right to establish the patentability of the claimed invention over any of the information provided herewith, and/or to prove that this information may not be prior art, and/or to prove that this information may not be enabling for the teachings purportedly offered.

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This statement should not be construed as a representation that a search has been

made, or that information more material to the examination of the present patent

application does not exist. The Examiner is specifically requested not to rely solely on

the material submitted herewith.

This Information Disclosure Statement is being filed before the mailing date of a

first Office Action on the merits. No statement or fee is required.

It is respectfully requested that the Examiner initial and return a copy of the

enclosed PTO-1449, and indicate in the official file wrapper of this patent application

that the documents have been considered.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee

deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Brian J. Del Buono Attorney for Applicants

Registration No. 42,473

Date:

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*Admitted only in Maryland *Admitted only in Virginia •Practice Limited to Federal Agencies

September 28, 2004

WRITER'S DIRECT NUMBER: (202) 772-8525 INTERNET ADDRESS: BRIAND@SKGF.COM

Art Unit 1641

Commissioner for Patents PO Box 1450 Alexandria, VA 22313-1450

Re:

U.S. Utility Patent Application

Application No. 10/743,295; Filed: December 23, 2003

For: Polymer Conjugates of Cytokines, Chemokines, Growth Factors,

Polypeptide Hormones and Antagonists Thereof with Preserved

Receptor-Binding Activity

Inventors:

BHASKARAN et al.

Our Ref:

2057.0060002/JAG/BJD

Sir:

Transmitted herewith for appropriate action are the following documents:

- 1. Information Disclosure Statement Under 37 C.F.R. § 1.97(b);
- 2. **36** pages of Form PTO-1449;
- 3. Copies of the non-U.S. cited documents (126 documents: AL1-AL5 and AR1-AR36);
- 4. First Supplemental Information Disclosure Statement Under 37 C.F.R. § 1.97(b);
- 5. **5** pages of Form PTO-1449;
- 6. Copies of the non-U.S. cited documents (14 documents: AM5, AN5 and AS36-AR40); and
- 7. One (1) return postcard.

It is respectfully requested that the attached postcard be stamped with the date of filing of these documents, and that it be returned to our courier. In the event that extensions of time are

Commissioner for Patents September 28, 2004 Page 2

necessary to prevent abandonment of this patent application, then such extensions of time are hereby petitioned.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Brian J. Del Buono Attorney for Applicants Registration No. 42,473

BJD/nef Enclosures

316325_1.DOC



Applicant.

FORM PTO-1449

FIRST SUPPLEMENTAL
MATION DISCLOSURE STATEMENT

ATTY.	DOCKET	NO.
2057.	0060002/	JAG/BJI

APPLICATION NO. 10/743,295

APPLICANT

BHASKARAN et al.

FILING DATE December 23, 2003 GROUP 1641

	U.S. PATENT DOCUMENTS											
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE					
	AA											
	AB											
	AC											
	AD						"					
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	AG8	4,766,106	08/23/1988	Katre et al.			01/25/1988					
	AH8	4,847,325	07/11/1989	Shadle et al.			01/20/1988					
	AI8	4,917,888	04/17/1990	Katre et al.			12/11/1987					
	АЈ8	6,638,500 B1	10/28/2003	El-Tayar et al.			10/30/2000					
	AK8	2004/0043002 A1	03/04/2004	El-Tayar et al.			08/28/2003					

	FOREIGN PATENT DOCUMENTS										
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION				
	AL						Yes No				
	AM5	EP 0 229 108 B1	06/06/1986	Europe			Yes No				
	AN5	WO 87/00056	06/06/1986	WIPO			Yes No				
	AO						Yes No				
	AP						Yes No				

			OTHER (Including Author, Title, Date, Pertinent Pages, etc.)
	AR		
	AS	36	Acharya, A.S., et. al., "Selectivity in the Modification of the α-Amino Groups of Hemoglobin on Reductive Alkylation with Aliphatic Carbonyl Compounds," J. Biol. Chem. 260:6039-6046, The American Society of Biological Chemistists, Inc. (1985)
	AT	36	Bayer, E., et. al., "Functionalization of Soluble Polymers: 4. Synthesis of Dichloro- and Di(4-Formylphenyloxyethyl) Poly(Oxyethylene)," Polymer Bulletin 8:585-592, Springer-Verlag (1982)
EXAMINER	-		DATE CONSIDERED

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GROUP 1641

	U.S. PATENT DOCUMENTS										
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	AA										
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	FOREIGN PATENT DOCUMENTS											
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION					
	AL						Yes No					
	AM						Yes No					
	AN						Yes No					
	AO						Yes No					
	AP						Yes No					

	Т		OTHER (Including Author, Title, Date, Pertinent Pages, etc.)
	AR	37	Bayer, E., et. al., "Functionalization of Soluble Polymers: 6. Preparation and Kinetic Aspects of Linear, Hydrophilic Aldehydes Based on Poly(Oxyethylene)," Polymer Bulletin 13:431-434, Springer-Verlag (1985)
	AS	37	Chamow, S.M., et. al., "Modification of CD4 Immunoadhesin with Monoethoxypoly(ethylene glycol) Aldehyde via Reductive Alkylation," Bioconjugate Chem. 5:133-140, American Chemical Society (1994)
	AT	37	Friedman, M., et. al., "Reductive Alkylation of Proteins with Aromatic Aldehydes and Sodium Cyanoborohydride," Int. J. Peptide Protein Res. 6:183-185, Munksgaard Internation Publishers (1974)
XAMINER	<u></u>		DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to

Applicant.

FIRST SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO. APPLICATION NO. 2057.0060002/JAG/BJD 10/743,295

APPLICANT
BUNGKARAN et al

BHASKARAN et al.

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U.S. PATENT DOCUMENTS											
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE				
	AA										
	AB										
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	FOREIGN PATENT DOCUMENTS											
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION					
	AL						Yes No					
*	AM						Yes No					
	AN						Yes No					
	AO						Yes No					
	AP						Yes No					

		1 1	OTHER (Including Author, Title, Date, Pertinent Pages, etc.)
	AR	38	Harris, J.M., et. al., "New Polyethylene Glycols for Biomedical Applications," in Water-Soluble Polymers: Synthesis, Solution Properties, and Applications, Shalaby, S.W., et al., eds., 198 th National Meeting of the American Chemical Society, Miami Florida, pp. 418-429 (1989)
,	AS	38	Harris, J.M., et. al., "Synthesis and Characterization of Poly(ethylene Glycol) Derivatives," Journal of Polymer Science 22:341-352, Polymer Chemistry Edition (1984)
	AT	38	Means, G.E., and Feeney, R.E., "Review: Reductive Alkylation of Proteins," Anal. Biochem. 224:1-16, Academic Press, Inc. (1995)

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	-		U.S. PA	ATENT DOCUMENTS	-		
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
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	FOREIGN PATENT DOCUMENTS						
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

	T	OTHER (Including Author, Title, Date, Pertinent Pages, etc.)
AR	39	Means, G.E., and Feeney, R.E., "Alkylating and similar reagents," in <i>Chemical Modification of Proteins</i> , Holden-Day, Inc., San Francisco, CA, pp. 105-138 (1971)
AS	39	Royer, G.P., "Immobilization of Enzymes on Aldehydic Matrices by Reductive Alyklylation," <i>Biochemical and Biophysical Research Communications 64</i> :478-484, Academic Press, Inc. (1975)
AT	39	Zalipsky, S., "Functionalized Polymers and Their Biologically-Relevant Conjugates," in Biomedical Functions and Biotechnology of Natural and Artificial Polymers, Yalpani, M., ed., ATL Press, Shrewsbury, MA, pp.63-76 (1996)

EXAMINER

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U.S. PATENT DOCUMENTS							
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA						
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	FOREIGN PATENT DOCUMENTS								
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION		
	AL						Yes No		
	AM						Yes No		
	AN						Yes No		
	AO						Yes No		
	AP						Yes No		

	-73			
			OTHER (Including Author, Title, Date, Pertinent Pages, e	tc.)
	AR	40	Copy of co-pending Taiwanese Application No. 92136592 et al., filed December 23, 1992 (NOT PUBLISHED)	, inventors Bhaskaran, S.S.,
	AS			
	АТ			
EXAMINER				DATE CONSIDERED

INFORMATION DISCLOSURE STATEMENT

FORM PTO-1449

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APPLICANT

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3. Met	/		U.S. PA	TENT DOCUMENTS			
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA1	4,002,531	01/11/1977	Royer			01/22/1976
	AB1	4,179,337	12/18/1979	Davis et al.			07/28/1977
	AC1	4,261,973	04/14/1981	Lee et al.			08/08/1977
	AD1	4,301,144	11/17/1981	Iwashita et al.			07/10/1980
	AE1	4,462,946	07/31/1984	Hanisch et al.			05/18/1983
	AF1	4,609,546	09/02/1986	Hiratani			06/23/1983
	AG1	4,732,863	003/22/1988	Tomasi et al.			12/31/1984
	AH1	4,816,440	03/28/1989	Thomson			09/26/1985
	AI1	4,894,330	01/16/1990	Hershenson et al.			12/23/1986
	AJ1	4,902,502	02/20/1990	Nitecki et al.			01/23/1989
	AK1	4,904,584	02/27/1990	Shaw			12/23/1987

FOREIGN PATENT DOCUMENTS								
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION	
	AL1	EP 0 098 110 B1	10/18/1989	Europe			Yes No	
	AM1	EP 0 733 067 B1	05/12/1999	Europe			Yes No	
	AN1	EP 1 039 922 B1	06/12/2002	Europe			Yes No	
	A01	EP 0 822 199 A2 and A3	02/04/1998	Europe			Yes No	
	AP1	WO 89/01033 A1	02/09/1989	WIPO			Yes No	

			OTHER (Including Author, Title, Date, Pertinent Pages, etc.)
	AR	1	Abuchowski, A., et al., "Immunosuppressive properties and circulating life of Achromobacter glutaminase-asparaginase covalently attached to polyethylene glycol in man," Cancer Treat Rep 65:1077-1081, Kluwer Academic (1981)
	AS	1	Abuchowski, A., et al., "Cancer therapy with chemically modified enzymes. I. Antitumor properties of polyethylene glycol-asparaginase conjugates," Cancer Biochem Biophys 7:175-186, Gordon & Breach (1984)
	AT	1	Abuchowski, A., et al., "Effect of covalent attachment of polyethylene glycol on immunogenicity and circulating life of bovine liver catalase," J Biol Chem 252:3582-3586, The American Society for Biochemistry and Molecular Biology (1977)
EXAMINER			DATE CONSIDERED

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APPLICATION NO. 10/743,295

APPLICANT

BHASKARAN et al.

FILING DATE December 23, 2003 GROUP 1641

·			U.S. P	ATENT DOCUMENTS		-	•
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA2	5,006,333	04/09/1991	Saifer et al.			07/13/1989
	AB2	5,080,891	01/14/1992	Saifer et al.			08/01/1990
	AC2	5,091,176	02/25/1992	Braatz et al.			04/24/1990
	AD2	5,122,614	06/16/1992	Zalipsky			04/19/1990
	AE2	5,206,344	04/27/1993	Katre et al.			01/11/1988
	AF2	5,219,564	06/15/1993	Zalipsky et al.			07/05/1991
-	AG2	5,252,714	10/12/1993	Harris et al.			11/28/1990
	AH2	5,281,698	01/25/1994	Nitecki			07/23/1991
	AI2	5,283,317	02/01/1994	Saifer et al.			10/11/1991
	AJ2	5,324,844	06/28/1994	Zalipsky			01/08/1992
	AK2	5,349,052	09/20/1994	Delgado et al.			05/12/1993

	FOREIGN PATENT DOCUMENTS								
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION		
	AL2	WO 89/05824 A1	06/29/1989	WIPO			Yes No		
	AM2	WO 92/16555 A1	10/01/1992	WIPO			Yes No		
	AN2	WO 96/40731 A1	12/19/1996	WIPO			Yes No		
	A02	WO 96/11953 A1	04/25/1996	WIPO			Yes No		
	AP2	WO 99/45026 A1	12/19/1996	WIPO			Yes No		

			OTHER (Including Author, Title, Date, Pertinent Pages, etc.)
	AR	2	Amoui, M., et al., "Differential phosphorylation of IRS-1 by insulin and insulin- like growth factor I receptors in Chinese hamster ovary cells," J Endocrinol 171:153-162, Society for Endocrinology (October 2001)
	AS	2	Arduini, R. M., et al., "Expression, purification, and characterization of rat interferon-beta, and preparation of an N-terminally PEGylated form with improved pharmacokinetic parameters," Protein Expr Purif 34: 229-242, Academic Press, Inc. (April 2004)
	АТ	2	Bailon, P., et al., "Rational design of a potent, long-lasting form of interferon: A 40 kDa branched polyethylene glycol-conjugated interferon alpha-2a for the treatment of hepatitis C," Bioconjug Chem 12:195-202, American Chemical Society (March-April 2001)
EXAMINER			DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to

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FORM PTO-1449 INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO. APPLICATION NO. 2057.0060002/JAG/BJD 10/743,295							
APPLICANT BHASKARAN et al.							
FILING DATE December 23, 2003	GROUP 1641						

			U.S. P	ATENT DOCUMENTS			
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	EAA.	5,362,852	11/08/1994	Geoghegan et al.			09/27/1991
	AB3	5,382,657	01/17/1995	Karasiewicz et al.			08/26/1992
	AC3	5,395,619	03/07/1995	Zalipsky et al.			03/03/1993
	AD3	5,449,090	08/29/1995	Harris			11/12/1993
	AE3	5,468,478	11/21/1995	Saifer et al.			10/18/1993
	AF3	5,476,653	12/19/1995	Pitt et al.			03/22/1995
	AG3	5,539,063	07/23/1996	Hakimi et al.			06/01/1995
	АНЗ	5,605,976	02/25/1997	Martinez et al.			05/15/1995
	AI3	5,612,460	03/18/1997	Zalipsky			02/17/1994
	AJ3	5,643,575	07/01/1997	Martinez et al.			10/27/1993
	AK3	5,672,662	09/30/1997	Harris et al.			10/02/1995

	FOREIGN PATENT DOCUMENTS									
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION			
	AL3	WO 99/55377 A2	11/04/1999	WIPO			Yes No			
	АМЗ	WO 99/58142 A1	11/18/1999	WIPO			Yes No			
	AN3	WO 00/07629 A2 and A3	02/17/2000	WIPO		\	Yes No			
	A03	WO 00/23114 A2 and A3	04/27/2000	WIPO			Yes No			
	AP3	WO 01/02017 A2 and A3	01/11/2001	WIPO			Yes No			

·			OTHER (Including Author, Title, Date, Pertinent Pages, etc.)
	AR	3	Bamborough, P., et al., "The interleukin-2 and interleukin-4 receptors studied by molecular modeling," Structure 2:839-851, Elsevier Science Ltd. (1994)
	AS	3	Basser, R.L., et al., "Development of pancytopenia with neutralizing antibodies to thrombopoietin after multicycle chemotherapy supported by megakaryocyte growth and development factor," Blood 99:2599-2602, The American Society of Hematology (April 2002)
	АТ	3	Bertolotto, A., et. al., "Differential effects of three interferon betas on neutralising antibodies in patients with multiple sclerosis: a follow up study in an independent laboratory," J. Neurol. Neurosurg. Psychiatry. 73:148-153, BMJ Publishing Group (April 2002)
EXAMINER			DATE CONSIDERED

INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO. 2057.0060002/JAG/BJD APPLICATION NO. 10/743,295

APPLICANT

FILING DATE December 23, 2003

BHASKARAN et al.

GROUP 1641

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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA4	5,681,567	10/28/1997	Martinez et al.			08/13/1996
	AB4	5,711,944	01/27/1998	Gilbert et al.			11/10/1994
	AC4	5,730,990	03/24/1998	Greenwald et al.			06/05/1995
	AD4	5,738,846	04/14/1998	Greenwald et al.			11/21/1995
	AE4	5,739,208	04/14/1998	Harris			06/07/1995
•	AF4	5,747,646	05/05/1998	Hakimi et al.			06/01/1995
	AG4	5,756,593	05/26/1998	Martinez et al.			06/27/1997
	AH4	5,770,577	06/23/1998	Kinslter et al.			11/14/1994
	AI4	5,792,834	08/11/1998	Hakimi et al.			06/01/1995
	AJ4	5,808,096	09/15/1998	Zalipsky			01/21/1997
	AK4	5,824,784	10/20/1998	Kinstler et al.			10/12/1994

			FOREIGN	PATENT DOCUMENTS			
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL4	WO 01/59078 A2 and A3	08/16/2001	WIPO .			Yes No
	AM4	WO 02/032957 A1	04/25/2002	WIPO	US.		X Yes No
	AN4	WO 02/049673 A2	06/27/2002	WIPO			Yes No
	A04	WO 03/031581 A2	04/17/2003	WIPO			Yes No
	AP4	WO 04/046222 A1	06/03/2004	WIPO			Yes X No

			OTHER (Including Author, Title, Date, Pertinent Pages, etc.)
	AR	4	Bowen, S., et al., "Relationship between molecular mass and duration of activity of polyethylene glycol conjugated granulocyte colony-stimulating factor mutein," Exp Hematol 27:425-432, Elsevier Science Inc. (1999)
	AS	4	Brenner, B.M., et al., "Glomerular permselectivity: Barrier function based on discrimination of molecular size and charge," Am J Physiol 234:F455-F460, American Physiological Society (1978)
	AT	4	Bruchelt, G., et al., "Determination of 2'-5'-oligoadenylate synthetase in serum and peripheral blood mononuclear cells before and after subcutaneous application of recombinant interferon beta and gamma," Eur J Clin Chem Clin Biochem 30:521-528, Walter de Gruyter & Co. (1992)
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	AA5	5,834,594	11/10/1998	Hakimi et al.			06/01/1995		
	AB5	5,849,860	12/15/1998	Hakimi et al.			06/01/1995		
	AC5	5,880,255	03/09/1999	Delgado et al.			04/14/1995		
	AD5	5,889,153	03/30/1999	Suzuki et al.			03/14/1997		
	AE5	5,900,461	05/04/1999	Harris			02/23/1998		
	AF5	5,902,588	05/11/1999	Greenwald et al.			11/19/1997		
	AG5	5,919,455	07/06/1999	Greenwald et al.			03/20/1997		
	AH5	5,932,462	08/03/1999	Harris et al.			05/17/1995		
	AI5	5,985,263	11/16/1999	Lee et al.			12/19/1997		
	AJ5	5,985,265	11/16/1999	Kinstler et al.			06/20/1997		
	AK5	5,990,237	11/23/1999	Bentley et al.			05/20/1998		

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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL5	WO 04/060299 A2	07/22/2004	WIPO			Yes No
	АМ						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

7		,	OTHER (Including Author, Title, Date, Pertinent Pages, etc.)
	AR	<u>5</u>	Brzozowski, A.M., et al., "Structural origins of the functional divergence of human insulin-like growth factor-I and insulin," Biochemistry 41:9389-9397, American Chemical Society (July 2002)
	AS	<u>5</u>	Bunn, P.A., et al., "Epidermal growth factor receptor expression, signal pathway, and inhibitors in non-small cell lung cancer," Semin Oncol 29:38-44, W.B. Saunders Company (October 2002)
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	AA6	6,042,822	03/28/2000	Gilbert et al.			04/06/1999
	AB6	6,077,939	06/20/2000	Wei et al.			08/04/1997
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	AD6	6,340,742 B1	01/22/2002	Burg et al.			06/28/2000
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	AL						Yes No
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	AR	<u>6</u>	Carpenter, G., et al., "Epidermal growth factor," J Biol Chem 265:7709-7712, The American Society for Biochemistry and Molecular Biology (1990)
	AS	<u>6</u>	Chander, G., et al., "Treatment of chronic hepatitis C: A systematic review," Hepatology 36:S135-S144, Wiley (November 2002)
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	AA8	2003/01505224 A1	06/05/2003	Roberts et al.			10/09/2001		
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AR	8	Clark, R., et al., "Long-acting growth hormones produced by conjugation with polyethylene glycol," J Biol Chem 271:21969-21977, The American Society for Biochemistry and Molecular Biology (1996)
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AR	9	Dixon, H.B.F., et al. "N-Terminal modification of proteins - A review," J Protein Chem 3:99-108, Plenum Publishing Corporation (1984)						
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	AL						Yes No		
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	AR	12	Grace, M., et al., "Structural and biologic characterization of pegylated recombinant IFN-alpha2b," J Interferon Cytokine Res 21:1103-1115, Mary Ann Liebert Inc. (December 2001)
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	AL						Yes No				
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	AR	13	Hinds, K., et al., "Synthesis and characterization of p conjugates," Bioconjug Chem 11:195-201, American Chemic	
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AR	14	Hymowitz, S.G., et al., "A unique zinc-binding site revealed by a high-resolution X-ray structure of homotrimeric Apo2L/TRAIL," Biochemistry 39:633-640, American Chemical Society (2000)
AS	14	Josephson, K., et al., "Design and analysis of an engineered human interleukin-10 monomer," J Biol Chem 275:13552-13557, The American Society for Biochemistry and Molecular Biology (2000)
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	AL						Yes No					
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	AL						Yes No						
	АМ						Yes No						
	AN						Yes No						
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	AP						Yes No						

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	AR	<u>17</u>	Knauf, M.J., et al., "Relationship of effective molecular size to systemic clearance in rats of recombinant interleukin-2 chemically modified with water-soluble polymers," J Biol Chem 263:15064-15070, American Society for Biochemistry and Molecular Biology (1988)
	AS	17	Kochendoerfer, G.G., et. al., "Design and Chemical Synthesis of a Homogeneous Polymer-Modified Erythropoiesis Protein," Science 299:884-887, American Association for the Advancement of Science (February 2003)
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	AS	19	Leong, S.R., et al., "Adapting pharmacokinetic properties of a humanized anti- interleukin-8 antibody for therapeutic applications using site-specific PEGylation," Cytokine 16:106-119, Academic Press, Inc. (November 2001)							
	AT	19	Li, J., et al., "Thrombocytopenia caused by the development of antibodies to thrombopoietin," Blood 98:3241-3248, American Society of Hematology (December 2001)							
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	AR	20	Lin, L., w	Betaseron,"	Dev Biol Stand 96:97-104	, Kargei	c (1998)		
·	AS	Lin, L.S., et al., "Interferon-beta-1b (Betaseron®): A model for hydrophobic therapeutic proteins," Pharm Biotechnol 9:275-301, Plenum Press (1996)							
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	AR	21	alfa-2b pl	us ribavirin	Peginterferon alfa-2b plus for initial treatment of -965, Lancet Publishing G	chronic h	epatitis C: A		
	AS	21	McNiece, I (1995)	.K., et al.,	"Stem cell factor," J Le	ukoc Biol	58:14-22, Wil	ey-Liss, Inc.	
	AT	21	Merrill, E.W., "Poly(ethylene oxide) star molecules: Synthesis, characterization, and applications in medicine and biology," J Biomater Sci Polymer Edn 5:1-11, VSP, The Netherlands (1993)						
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	AS	Monkarsh, S.P., et al., "Isolation of positional isomers of mono-poly(ethylene glycol)ylate interferon/alpha-2a and the determination of their biochemical and biological characteristics," in Harris, J.M., et al., eds., Poly(ethylene glycol) Chemistry and Biological Applications, American Chemical Society, Washington, D.C pp. 207-216 (1997)						
	AT	22	Mordenti, data for f Corporatio	ive therapeu	"Interspecies scaling of tic proteins," Pharm Res	clearance 8:1351-135	and volume of	distribution
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	AS	23	Morris, J.C., et al., "Advances in interleukin 2 receptor targeted treatment," Ann Rheum Dis 59 (Suppl I):i109-i114, BMJ Publishing Group Ltd. (2000)							
·	AT	23	Morrissey, P.J., et al., "Steel factor (c-kit ligand) stimulates the in vitro growth of immature CD3-/CD4-/CD8- thymocytes: Synergy with IL-7," Cell Immunol 157:118-131, Academic Press, Inc. (1994)							
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	AS	25	glycol-mod J Pharmaco	ified form of 1 Exp Ther 25	"Improved pharmacoking interferon-beta-la wi 97:1059-1066, American ics (June 2001)	th preserved	in vitro bio	activity,"
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	AS	26	antibodies		novel bioassay for the dlb." J Interferon Cytok					
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	AS	27	Ross, R.J.M., et al., "Binding and functional studies with the growth hormone receptor antagonist, B2036-PEG (pegvisomant), reveal effects of pegylation and evidence that it binds to a receptor dimer," J Clin Endocrinol Metab 86:1716-1723, The Endocrine Society (April 2001) Rostaing, L., et al., "Pharmacokinetics of alphaIFN-2b in chronic hepatitis C virus patients undergoing chronic hemodialysis or with normal renal function: Clinical implications," J Am Soc Nephrol 9:2344-2348, Lippincott Williams & Wilkins (1998)						
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	AS	Thiel, D.J., et al., "Observation of an unexpected third receptor molecule in the crystal structure of human interferon-gamma receptor complex," Structure 8:927-936, Elsevier Science Ltd. (2000)						
	AT	Utsumi, T., et al., "The role of amino functions in recombinant human tumor necrosis factor in expression of biological activity," Mol Immunol 29:77-81, Pergamon Press, (1992)						
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	AS	Wadhwa, M., et al., "Immunogenicity of granulocyte-macrophage colony-stimulating factor (GM-CSF) products in patients undergoing combination therapy with GM-CSF," Clin Cancer Res 5:1353-1361, The American Association for Cancer Research (1999)						
	AT	Walter, M.R., et al., "Crystal structure of a complex between interferon-gamma and its soluble high-affinity receptor," Nature 376:230-235, Macmillan Magazines Ltd. (1995)						
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